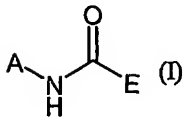
Claims

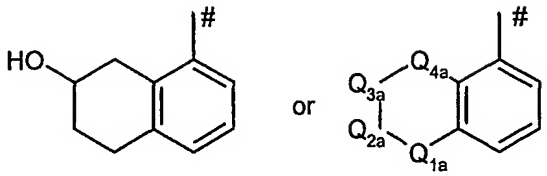
1. A compound of the formula (I), their tautomeric and stereoisomeric form, and salts thereof:



(I)

wherein

A represents the formula



wherein

represents the connection position to the molecule,

Q_{1a} and Q_{4a} independently represent direct bond or methylene,

Q_{2a} represents CHR^{2a},

Q_{3a} represents CHR^{3a},

wherein

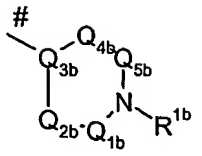
R^{2a} represents hydrogen, hydroxy, C_{1-6} alkoxy or C_{1-6} alkanoyloxy, and

R^{3a} represents hydrogen, hydroxy, C_{1-6} alkoxy, or C_{1-6} alkanoyloxy,

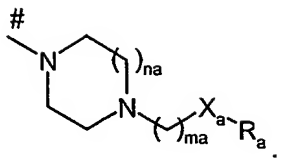
with the proviso that Q_{1a} and Q_{4a} can not be direct bond at the same time and R^{2a} and R^{3a} can not be hydrogen at the same time,

and

E represents the formula



or



wherein

represents the connection position to the molecule,

Q_{1b}, Q_{2b}, Q_{4b} and Q_{5b} independently represent $C(R^{11b})(R^{12b})$,

wherein

R^{11b} and R^{12b} independently represent hydrogen, phenyl, benzyl, or C_{1-6} alkyl optionally substituted by hydroxy, carboxy, phenyl, benzyl, C_{1-6} alkoxy, C_{1-6} alkoxycarbonyl, C_{1-6} alkylamino, or di(C_{1-6} alkyl)amino;

Q_{3b} represents $C\text{-}R^{13b}$,

wherein

R^{13b} represents hydrogen, phenyl, benzyl, or C_{1-6} alkyl optionally substituted by hydroxy, carboxy, phenyl, benzyl, C_{1-6} alkoxy, C_{1-6} alkoxycarbonyl, C_{1-6} alkylamino, or di(C_{1-6} alkyl)amino;

R^{1b} represents C_{1-6} alkyl substitiuted by aryl or heteroaryl,

wherein

said aryl and heteroaryl are optionally substituted with one or more substituents selected from the group consisting of halogen, nitro, hydroxy, C_{1-6} alkylamino, di(C_{1-6} alkyl)amino, C_{3-8} cycloalkylamino, C_{1-6} alkoxycarbonyl, phenyl, benzyl, heterocycle, sulfonamide, C_{1-6} alkanoyl, C_{1-6} alkanoylamino, carbamoyl, C_{1-6} alkylcarbamoyl, cyano, C_{1-6} alkyl optionally substituted by cyano, C_{1-6} alkoxycarbonyl or mono-, di-, or tri-halogen, C_{1-6} alkoxy optionally substituted by mono-, di-, or tri- halogen, phenoxy optionally substituted by halogen or C_{1-6} alkyl, or C_{1-6} alkylthio optionally substituted by mono-, di-, or tri- halogen, C_{3-8} cycloalkyl, and heterocycle;

or

aryl or heteroaryl,

wherein

said aryl and heteroaryl are optionally substituted with one or more substituents selected from the group consisting of halogen, nitro, hydroxy, C_{1-6} alkylamino, di(C_{1-6} alkyl)amino, C_{3-8} cycloalkylamino, C_{1-6} alkoxycarbonyl, phenyl, benzyl, heterocycle, sulfonamide, C_{1-6} alkanoyl, C_{1-6} alkanoylamino, carbamoyl, C_{1-6} alkylcarbamoyl, cyano, C_{1-6} alkyl optionally substituted by cyano, C_{1-6} alkoxycarbonyl or mono-, di-, or tri-halogen, C_{1-6} alkoxy optionally substituted by mono-, di-, or tri- halogen, phenoxy optionally substituted by halogen or C_{1-6} alkyl, or C_{1-6} alkylthio optionally substituted by mono-, di-, or tri- halogen, C_{3-8} cycloalkyl, and heterocycle;

na represents 1 or 2;

ma represents 0, 1, 2, or 3 ;

$-X_a-$ represents bond, -O- or $-N(R^{1a})-$ (wherein R^{1a} is hydrogen or C_{1-6} alkyl);

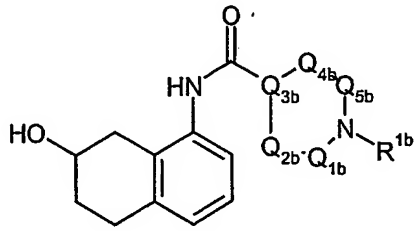
and

R_a represents aryl or heteroaryl

Wherein said aryl and heteroaryl are optionally substituted with one or more substituents independently selected from the group consisting of halogen, nitro, hydroxy, carboxy, amino, C_{1-6} alkylamino, di(C_{1-6} alkyl)amino, C_{3-8} cycloalkylamino, C_{1-6} alkoxycarbonyl, phenyl (which phenyl is optionally substituted by halogen, nitro, hydroxy, carboxy, amino, C_{1-6} alkylamino, di(C_{1-6} alkyl)amino, C_{3-8} cycloalkylamino, or C_{1-6} alkoxycarbonyl), benzyl (in which phenyl moiety is optionally substituted by halogen, nitro, hydroxy, carboxy, amino, C_{1-6} alkylamino, di(C_{1-6} alkyl)amino, C_{3-8} cycloalkylamino, or C_{1-6} alkoxycarbonyl), sulfonamide, C_{1-6} alkanoyl, C_{1-6} alkanoylamino, carbamoyl, C_{1-6} alkylcarbamoyl, cyano, C_{1-6} alkyl (which alkyl is optionally substituted by cyano, nitro, hydroxy, carboxy, amino, C_{1-6} alkoxycarbonyl or mono-, di-, or tri-halogen), C_{1-6} alkoxy (which alkoxy is optionally substituted by mono-, di-, or tri- halogen), phenoxy (in which phenyl moiety is optionally substituted by halogen, nitro, hydroxy, carboxy, amino, C_{1-6} alkylamino, di(C_{1-6} alkyl)amino,

C_{3-8} cycloalkylamino, or C_{1-6} alkoxycarbonyl or C_{1-6} alkyl), C_{1-6} alkylthio (which alkylthio is optionally substituted by mono-, di-, or tri- halogen), C_{3-8} cycloalkyl, and heterocycle.

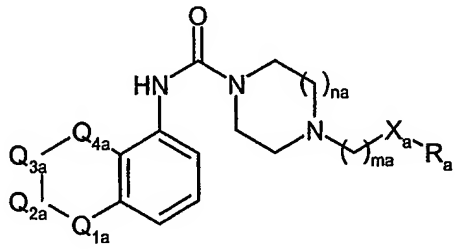
2. Compound of formula (I) according to claim 1, with the formula (Ib), their tautomeric and stereoisomeric form, and salts thereof:



(Ib)

wherein Q_{1b}, Q_{2b}, Q_{3b}, Q_{4b}, Q_{5b} and R^{1b} are the same as defined in claim 1.

3. Compound of formula (I) according to claim 1, with the formula (Ia), their tautomeric and stereoisomeric form, and salts thereof:

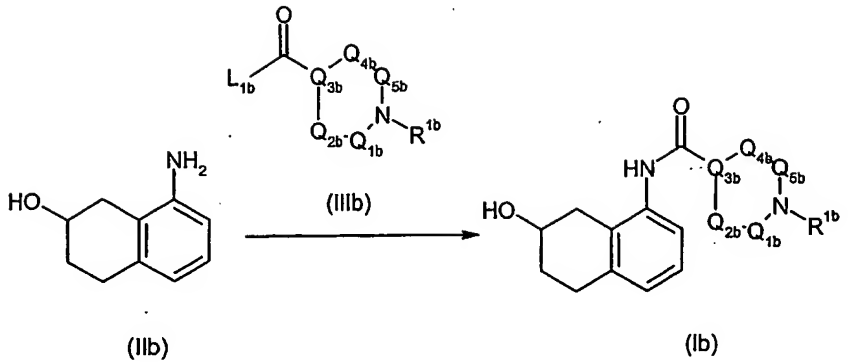


(Ia)

wherein Q_{1a}, Q_{2a}, Q_{3a}, Q_{4a}, na, ma, X_a and R_a are the same as defined in claim 1.

4. A process for synthesizing the compounds of general formula (I), wherein formula (I) contains the compounds of formula (Ib) and (Ia), according to claim 1, characterized in that

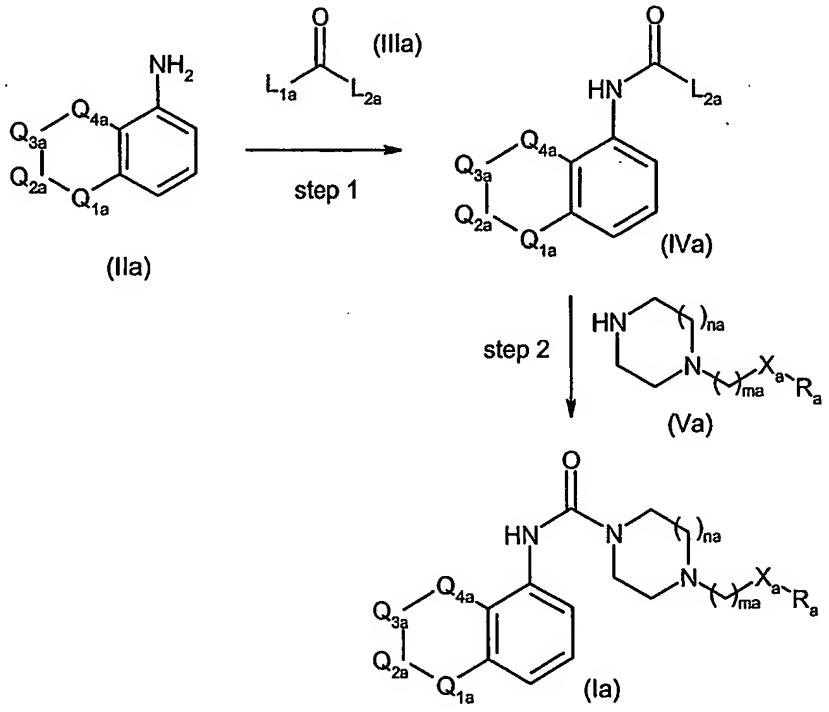
[Method Ab]



a compound of the formula (Ib), wherein Q_{1b}, Q_{2b}, Q_{3b}, Q_{4b}, Q_{5b} and R^{1b} are the same as defined in claim 1, can be prepared by the reaction of the compound of the formula (IIb) with the compound of the formula (IIIb), wherein Q_{1b}, Q_{2b}, Q_{3b}, Q_{4b}, Q_{5b} and R^{1b} are the same as defined in claim 1, and L_{1b} represents a leaving group including, for instance, hydroxy, halogen atom such as chlorine, bromine, or iodine atom, or azole such as imidazole or triazole,

or

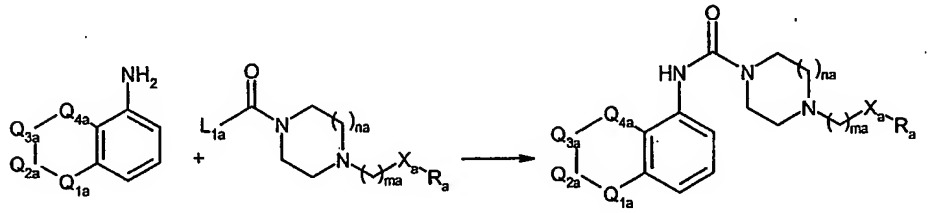
[Method Aa]



a compound of the formula (IVa), wherein Q_{1a}, Q_{2a}, Q_{3a}, and Q_{4a}, are the same as defined in claim 1, can be prepared by the reaction of the compound of the formula (IIa), wherein Q_{1a}, Q_{2a}, Q_{3a}, and Q_{4a}, are the same as defined in claim1, with the compound of the formula (IIIa), wherein L_{1a} represents a leaving group including, for instance, hydroxy, halogen atom such as chlorine, bromine, or iodine atom, or azole such as imidazole or triazole and L_{2a} represents a leaving group including, for instance, halogen atom such as chlorine, bromine, or iodine atom, or phenoxy, and then the compound of the formula (Va), wherein na, ma, X_a and R_a are the same as defined in claim 1, is reacted with the compound (IVa) to obtain the compound of the formula (Ia), wherein Q_{1a}, Q_{2a}, Q_{3a}, Q_{4a}, na, ma, X_a and R_a are the same as defined in claim 1,

or

[Method Ba]

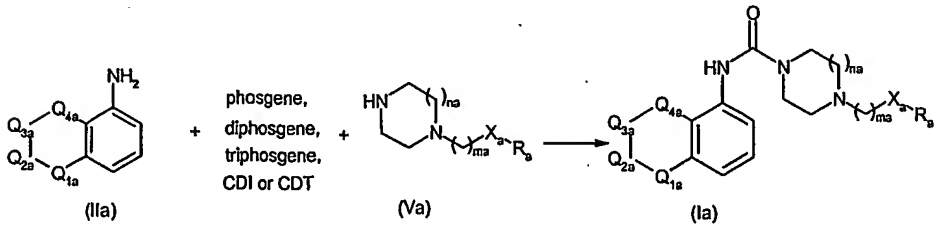


(IIa) (VIa) (Ia)

a compound of the formula (Ia) can be prepared by the reaction of the compound of the formula (IIa) and the compound of the formula (VIa), wherein na, ma, X_a, R_a and L_{1a} are the same as defined in claim 1,

or

[Method Ca]



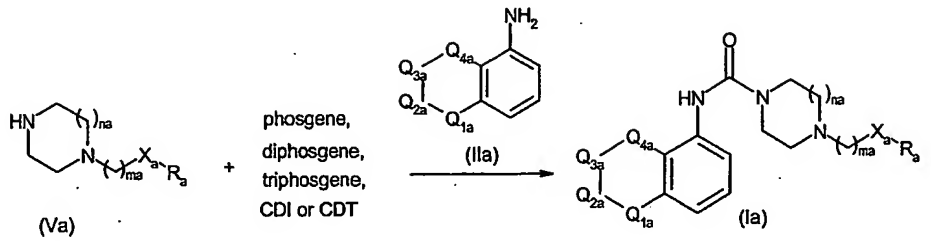
(IIa) (Va) (Ia)

a compound of the formula (Ia) can be prepared by reacting the compound of the formula (IIa) with phosgene, diphosgene, triphosgene, 1,1-carbonyldiimidazole (CDI), or 1,1'-

carbonyldi(1,2,4-triazole)(CDT), and then adding the compound of the formula (Va) to the reaction mixture,

or

[Method Da]



a compound of the formula (Ia) can be prepared by reacting the compound of the formula (Va) with phosgene, diphosgene, triphosgene, 1,1-carbonyldiimidazole (CDI), or 1,1'-carbonyldi(1,2,4-triazole)(CDT) and then adding the compound of the formula (IIa) to the reaction mixture.

5. A medicament comprising the derivative of the formula (I), its tautomeric or stereoisomeric form, or a physiologically acceptable salt thereof as claimed in claim 1 as an active ingredient.

6. The medicament as claimed in claim 4, further comprising one or more pharmaceutically acceptable excipients.

7. The medicament as claimed in claim 4, wherein said derivative of the formula (I), its tautomeric or stereoisomeric form, or a physiologically acceptable salt thereof is a VR1 antagonist.

8. The medicament as claimed in claim 4 for the treatment and/or prevention of an urological disorder or disease.

9. The medicament as claimed in claim 7, wherein said urological disorder or disease is detrusor overactivity (overactive bladder), urinary incontinence, neurogenic detrusor oeractivity (detrusor hyperflexia), idiopathic detrusor overactivity (detrusor instability), benign prostatic hyperplasia, and lower urinary tract symptoms.

10. The medicament as claimed in claim 4 for the treatment and/or prevention of pain.

11. The medicament as claimed in claim 9, wherein said disorder or disease realted to pain is neuralgia, neuropathies, algesia, nerve injury, ischaemia, neurodegeneration, or stroke.

12. The medicament as claimed in claim 4 for the treatment and/or prevention of an inflammatory disorder or disease.

13. The medicament as claimed in claim 11, wherein said inflammatory disorder or disease is asthma or COPD.

14. Use of compounds according to claim 1 for manufacturing a medicament for the treatment and/or prevention of an urological disorder or disease.

15. Use of compounds according to claim 1 for manufacturing a medicament for the treatment and/or prevention of pain.

16. Use of compounds according to claim 1 for manufacturing a medicament for the treatment and/or prevention of an inflammatory disorder or disease.

17. Process for controlling an urological disorder or disease in humans and animals by administration of a VR1-antagonistically effective amount of at least one compound according to claim 1.

18. Process for controlling pain in humans and animals by administration of a VR1-antagonistically effective amount of at least one compound according to claim 1.

19. Process for controlling an inflammatory disorder or disease in humans and animals by administration of a VR1-antagonistically effective amount of at least one compound according to claim 1.